# Gut microbiota and surgical disease

# **Bengt Jeppsson**

Department of Surgery, Lund University, Lund, Sweden

*Correspondence to:* Bengt Jeppsson MD, PhD, FRCS (Engl). Professor of Surgery, Department of Surgery, Lund University, Lund, Sweden. Email: bengt.jeppsson@med.lu.se.

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Why should surgeons study gut microbiota and microbiome (totality of body's microorganisms and genomes)? There are at least three reasons. With the advent of new ways of analyzing gut microbiome it may soon be possible to use in diagnosis of clinical conditions. Secondly, knowledge of microbiome will give insights into the pathophysiology of trauma and surgical conditions and thirdly, new microbiome-based therapies are emerging.

The gut microbiome can be considered a new organ in our body. Traditionally we have considered bacteria as friendly commensals or harmful pathogens. This separation of the two is no longer sharp and the intestinal microbiome is a complex entity in which species can shift sides—from friend to foe and return based on important factors in the local environment. We have long believed that our body contains more bacterial cells than human eukaryotic cells but new data show that we are made up of as many bacterial cells as human cells (about a 1:1 ratio) (1). Vital functions of the gut microbiota include conversion of otherwise indigestible food components, production of essential cofactors and vitamins, modulation of gut barrier integrity, regulation of gastrointestinal peptide hormone secretion and stimulation of the innate immune system.

The development of the human microbiome begins very early in life and is dependent on surrounding factors. Early on after delivery the bacterial communities become distinct. Several medical and surgical problems are coupled to perturbations of the microbiome. The physiologic perturbations caused by surgical stress along with selective pressures imposed by antibiotics, hypoxia and nutrient depletion alter the microbial balance in the gut (2). The majority of data are derived from faecal samples and to lesser extent mucosal biopsies. While it is relatively easy to obtain fresh faecal samples, the information obtained from them does not represent the complete picture in the gut and the mucosa-associated microbiota (3). This may be one reason for the great variability of results from different studies and microbiome-based therapies. While the development of the human microbiome is affected by early bacterial exposure, the adult microbiome is relatively stable. The intestinal microbiome can fluctuate on a daily basis, sometimes even shorter. Life-style factors e.g., diet, exercise, smoking, environment and pets affect the microbiome. Intake of drugs and especially antibiotics has a profound influence and recovery may take many months and is often incomplete. A significant disruption of the homeostasis of the microbiome, a phenomenon called dysbiosis, may contribute to the onset of many disorders; whereas increased microbial diversity is associated with a beneficial impact (4). The microbiome plays an important role in the regulation of systemic inflammation. Many clinical conditions in surgery are accompanied with increased inflammation.

How can we target the microbial community? The most drastic action is faecal microbial transplantation. The first evidence of the use of this treatment has been found in Chinese medicine during the fourth century by Ge Hong (4). In this mode of therapy not only microbes are transplanted but also bacteriophagic particles, viruses, fungi and archaea, which may carry risks in sick patients with a compromised immune function. It has not yet been used in surgical patients besides to combat recurrent clostridial infections. Administration of prebiotics, i.e., different fibers to stimulate microbial growth is another approach.

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Thereby an increased production of e.g., butyrate could be achieved and low levels of butyrate are often encountered in surgical patients. The use of fibers has not systematically been studied in this context, probably since the effect of administration is slow. The administration of live bacteria (probiotics) has been tried in several clinical trials in preoperative regimens (5) and in intensive care patients with multiple organ failure (6). Different lactobacilli have most often been used. It has been shown that probiotics with specific characteristics have the ability to colonize the gastrointestinal tract after oral administration and alter the ecology in patients where antibiotics have failed. The approach seems attractive especially in the era of increasing resistance to antibiotics. It is, however, important to know the specifics of the bacteria used down to species level and continually monitor for side effects. Other and newer sources of probiotics are under development such as engineered commensals with enhanced capacity to fight pathogens.

What can we surgeons do to reduce the negative impact on gut microbiota in surgical patients?

We must question if mechanical bowel preparation in many situations is necessary, well aware of the long time restoration of healthy gut microbiota may take. More studies are needed.

We must also refine the use of prophylactic antibiotics to reduce the impact on the resident flora. More research is needed regarding dose used, timing of administration in relation to surgery and duration of prophylaxis.

We must further try to minimize the surgical trauma, inflammatory response and stress, which all may have a negative impact on gut microbiota. We must continue to study effects on gut microbiota in relation to surgical technique. What difference does the use of minimal invasive procedures compared to traditional surgery in this aspect? Many questions need to be answered.

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We are finally starting to envision how we can develop knowledge of the "new organ" that gut microbiota and microbiome constitute and utilize the knowledge to improve care of surgical patients.

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### Footnote

*Conflicts of Interest*: B Jeppsson works as a senior advisor for Probi AB, Lund, Sweden.

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